REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-16 are in this Application. Claims 9-16 have been withdrawn from consideration. Claims 1-8 have been rejected under 35 U.S.C. § 112. Claims 1-4 have been rejected under 35 U.S.C. § 102(b). Claims 1-3 have been rejected under 35 U.S.C. § 102(e). Claims 1-3, 7 and 8 have been rejected under 35 U.S.C. § 103(a). New claims 17 and 18 have now been added. Claims 1, 2 and 5-8 have been amended herewith.

35 U.S.C. § 112, 1st paragraph Rejections

The Examiner has rejected claims 1-8 under 35 USC 112, 1st paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventor had possession of the claimed invention. Applicant respectfully traverses the Examiner's rejections. Claims 1, 2, and 5-8 have now been amended.

The Examiner has asserted that while the claims are drawn to constructs comprising sequences and genes conferring mitigating genetic traits deleterious to weeds, and benign or advantageous when expressed in the commercially cultivated crop, and the use thereof for transforming crop plants, the specification provides no guidance regarding "...isolation of any protein (or other gene product) from any source or of any sequence..." which would confer the mitigating trait. Further, the Examiner asserts that the specification fails to provide any method of using such a sequence for transforming plant cells and plants. Applicant vigorously disagrees.

Applicant wishes to point out that the claims before the Examiner are directed toward methods of obtaining a cultivated crop capable of mitigating the effects of disadvantageous and undesirable intra- or interspecies introgression by interbreeding of genetically engineered trait(s) from the transgenic crops to an uncultivated, interbreeding species of the crop by using genetic constructs having tightly linked advantageous and mitigating traits capable of tandem introgression, for mitigating the spread, as a result of accidental genetic transfer, of advantageous traits such as herbicide resistance, environmental stress resistance, high productivity, genetically

engineered pharmaceuticals, pollutant phytoremediation, etc. to related undesirable, uncultivated species of the crop. Thus, in contrast to the Examiner's assertion, the claimed method teaches the use of constructs comprising both advantageous and mitagating traits in tight genetic linkage, wherein the mitigating trait(s) are disadvantageous to the uncultivated interbreeding species related to the cultivated crop. A detailed, respresentative listing of examples of such tandem constructs having both the advantageous and mitigating traits is provided in Table 4 (page 54 of the instant specification) and throughout the specification.

The Examiner asserts that the specification "provides no guidance" regarding the sequences conferring the mitigating traits, sources thereof, methods for their use in constructs for plant transformation, or evaluation of putative "advantageous" or "mitigating" genes. Applicant disagrees.

Applicant wishes to point out that Table 2 (pages 20-22 of the instant specification), Table 3 (pages 22-23 of the instant specification), Table 5 (pages 74-76 of the instant specification), Table 6 (page 81 of the instant specification); Table 7 (pages 86-87 of the instant specification) and Table 8 (pages 90-91 of the instant specification) list numerous advantageous traits for culitvated crop transformation, and the gene sequences or sources thereof useful for transformation. Suitable mitigating traits, and the sequences thereof, to be used in tight genetic linkage with the advantageous traits, are disclosed in detail in the instant specification, for example, secondary dormancy (see page 43, line 29- page 44, line 27), uniform ripening/anti-shattering (see page 46, line 28- page 47, line 28), dwarfing (see page 47, line 29-page 48, line 28), and bolting (see page 48, line 29-page 49, line 17. Specific mitigating sequences disclosed include, for example, *"shatterproof"*; gai; O,GRF1; phytochrome B, brassinosteroids, and GA_1 and GA_4. Further, mitigating sequences and constructs uniquely suited for individual crops are described (see Example 1 for tobacco, Example 2 for oilseed rape, Example 3 for corn, Example 4 for rice, Example 5 for root crops and Example 6 for trees).

The Examiner has further asserted that the "single exemplified dwarfism trait was deleterious to the crop", and that the "unpredictability inherent in the process" is demonstrated by Al-Ahmad et al (2004). Applicant strongly disagrees.

Firstly, regarding Al-Ahmad et al, Applicant believes that the Examiner has misinterpreted the cited reference. In the abstract, Al-Ahmad concludes that:

> "The results demonstrate the suppression of crop-weed hybrids when competing with wild type weeds, or such crops as volunteer weeds, in seasons when the selector (herbicide) is not used. The linked unfitness would be continuously manifested in future generations, keeping the transgene at a low frequency."

More significantly, Applicant believes that the Examiner has overlooked the abundant enablement and support provided in the instant specification. Examples 1 and 2 detail the reduction to practice of the claimed method. Artificial introgression (by transformation) of a tandem construct containing an *ahas*^{R} (acetohydroxy acid synthase) gene (GenBank Accession No. X51514) for herbicide resistance as the primary desirable gene, and the dwarfing Δ*gai* (gibberellic acid-insensitive) mutant gene as a mitigator into tobacco (Example 1) and *brassica* (oilseed rape) plants, and the comparison of the growth of the resultant transgenic plants as "crops" (under "cultivated" conditions, or grown alone) and as uncultivated, interbreeding species (under "uncultivated" conditions, grown with wild type and in a variety of spacing) are disclosed.

The results surprisingly indicated that expression of the "advantageous" trait was evident when the genetically engineered test plants were grown alone (i.e. as the "crop plant"). However, in contrast, when the same plants were grown in competition with wild type plants (simulating the accidental introgression of the tandem constructs into an "uncultivated, closely related interbreeding species"), expression of the "mitigating" traits led to clearly impaired growth and reproductive fitness of both the transgenic tobacco and oilseed rape plants.

Example 1 shows that the dwarf and imazapyr resistant TM transgenic hybrid tobacco plants (simulating a TM introgressed hybrid) were more productive than the wild type when cultivated alone. They formed many more flowers than the wild type, which is an indication of a higher harvest index (Figure 2). Conversely, the TM transgenics were weak competitors and highly unfit when co-cultivated with the wild type in ecological simulation competition experiments (Figures 2,3). The lack of flowers on the TM plants in the competitive situation (Figure 2) led to a zero

reproductive fitness of the TM plants grown in a 1:1 mixture with the wild type at the spacings used, which are representative of those of weeds in the field (Figure 2). The highest vegetative fitness was less than 30% of the wild type (Figure 3).

Example 2 shows that the dwarf and imazapyr resistant TM transgenic hybrid oilseed rape plants (simulating a TM introgressed hybrid) were superior to wild type plants in growth and productivity (see Figure 7). All the TM Brassica crops, hybrids, and backcrosses (BC) with the wild type weedy *B. campestris* had similar dwarf phenotypes, characterized by delayed growth and flowering. The transgenic TM plants had more abundant, darker green, and thicker leaves, and thicker stems than those of the non-transgenic biotypes. The transgenic TM crops were more productive than the non-transgenic plants when grown alone, and the dry weight of total fully developed seeds per TM plant was greater than that of the non-transgenics. In contrast, both the transgenic TM heterozygous and homozygous transgenic *B. napus* plants were weak competitors when co-cultivated with the non-transgenic crop plants in ecological competition experiments (see Figure 8): by the time the non-transgenics had finished flowering and formed many siliques, all the surviving TM plants cultivated at 2.5-cm spacing failed to flower and had formed only very small canopies, indicating that the reproductive fitness of the TM plants was much lower than that of the non-transgenic competing plants. Significantly, it was observed that those TM plants successful in forming weak flower buds at 5-cm spacing were only those growing close to the edges of the containers, able to receive more light than those growing in the middle of the containers. However, both the weakly flowering and the non-flowering transgenic TM plants failed to produce mature siliques or viable seeds.

Yet further, introduction of the *Arabidopsis* "shatterproof" gene as a second mitigator sequence into *brassica*, designed to further inhibit undesirable spread of advantageous traits by random introgression into undesirable species, was successful in overcoming the high levels of seed shattering characteristic of wild *brassica* and producing transgenic plants having uniform seed dispersal (page 73, lines 1-13 of the instant specification).

Thus, in contrast to the Examiner's assertions, the instant specification defines and provides detailed description of primary, "advantageous" traits, suitable "mitigating" traits, combinations thereof and methods for their use, suitable for use

with a broad variety of crop species. Yet further in contrast to the Examiner's assertions, the instant inventors have successfully reduced the method of the present invention to practice, and show, in Examples 1 and 2, the unrestrained beneficial effect of an "advantageous" trait under "cultivated" crop conditions, along with the effective inhibition of growth, reproductive fitness and productivity of the transgenic plants expressing the tandem constructs, under competitive conditions simulating "uncultivated" growth.

The Examiner has further stated that no guidance is provided regarding the identification of any weedy species or transformation therewith to confer a deleterious trait thereto. Applicant wishes to point out that the claimed method is directed to obtaining a crop plant capable of mitigating the effects of unintended introgression of "desirable", "beneficial" traits into uncultivated, interbreeding species thereof, and has been shown, in the instant specification (see Example 2) to be efficacious as a mitigating system with the pernicious weedy species *Brassica campestris*. It will be appreciated, that prevention of introgression of genetically engineered traits such as herbicide resistance, is desirable for <u>all</u> interbreeding species not under cultivation along with the desired crop plant species, and it is by virtue of the essential feature of tight genetic linkage that tandem transformation and expression of both the "advantageous" desirable trait(s) and the "mitigating" trait(s) are ensured in the event of such unintentional introgression.

The abovementioned notwithstanding, Applicant wishes to direct the Examiner's attention to the numerous and detailed examples provided in the instant specification of undesirable interbreeding species problematic to the cultivation of specific crops such as oilseed rape, corn, rice, beets, etc.

In view of the numerous examples of "advantageous" and "mitigating" traits, and methods for their use disclosed in the instant specification, identification, isolation and evaluation of genes conferring "mitigating" traits would not require undue experimentation by one of ordinary skill in the art.

Thus, the Applicant respectfully requests withdrawal of the 35 U.S.C. 112, 1st paragraph rejections.

35 U.S.C. § 102 Rejections: WO 96/34088 (COLD SPRING HARBOR), WANG et al., LEE et al. (US 5,948,956)

The Examiner has rejected claims 1-4 under 35 USC§102(b), as being anticipated by WO96/34088 (COLD SPRING HARBOR) and WANG et al., and under 35 USC§102(e) as being anticipated by LEE et al (US 5,948,956). Claims 1 and 2 have now been amended. The Examiners rejections are respectfully traversed.

The Examiner states that WO96/34088 teaches dicot or maize plants transformed with a genetic construct comprising a first gene encoding herbicide resistance linked to a second gene encoding an antisense Id mRNA, resulting in non-flowering in the plants, thereby anticipating the claimed invention. Applicant disagrees.

The present invention is of a method for mitigating the effects of disadvantageous and undesirable intra- or interspecies introgression by interbreeding of genetically engineered trait(s) from the transgenic crops to an uncultivated, interbreeding species of the crop by using genetic constructs having tightly linked advantageous and mitigating traits capable of tandem introgression, for mitigating the spread, as a result of accidental genetic transfer, of advantageous traits such as herbicide resistance, environmental stress resistance, high productivity, genetically engineered pharmaceuticals, pollutant phytoremediation, etc. to related undesirable, uncultivated species of the crop. In contrast, WO96/34088 teaches the identification, cloning and sequencing of the *Id* gene from maize, and overexpression or repression (by anti-sense mRNA) of the *Id* gene, for control of flowering in plants. No reduction to practice, no transformation of plants with any genetic construct and no plants with absent flowers are disclosed. WO96/34088 is silent regarding introgression or prevention of introgression of transgenic traits.

Further, WO96/34088 provides merely prophetic examples of the use of constructs comprising the *Id* gene for control of flowering in crop plants, with the optional use of a herbicide resistance gene for a selective marker:

> "Transgenic plants carrying the construct are examined for the desired phenotype using a variety of methods including but not limited to an appropriate phenotypic marker, such as antibiotic resistance or herbicide resistance, or visual observation of the time of floral induction compared to

naturally-occurring plants."(WO96/34088, page 22, lines 14-20)

Thus, WO96/34088 is silent regarding selection of a mitigating trait detrimental to an uncultivated, interbreeding species, and not detrimental to a cultivated species of the crop, and as such lacks the essential features of the method of the present invention, as recited in now amended claim 1:

> "...method of obtaining a transformed, cultivated crop capable of mitigating the effects of introgression of at least one advantageous genetically engineered trait to an uncultivated interbreeding species related to the transformed cultivated crop, the method comprising transforming a population of plants of the cultivated crop to co-express the at least one advantageous genetically engineered, trait, and at least one, mitigating genetic trait, wherein:
> said advantageous genetic trait is selected beneficial to said crop;
> said mitigating genetic trait is selected detrimental to the uncultivated interbreeding species and not detrimental to said crop;
> whereas said advantageous genetically engineered trait and said mitigating genetic trait being tightly genetically linked so as to produce tandem introgression of said advantageous and said mitigating traits into said uncultivated interbreeding species ..."

Thus, WO96/34088 does not, and cannot anticipate the invention as recited in amended claim 1, and claims dependent therefrom of the present invention.

The Examiner has further rejected claims 1-4 as anticipated by Wang et al. The Examiner asserts that Wang et al teach plant transformation with a genetic construct comprising a gene encoding herbicide resistance linked to a second gene encoding CCA-1 protein, producing plants absent flowers. Applicant believes that the Examiner has misunderstood the cited reference. Wang et al. is a research publication reporting the transgenic, constitutive expression of a circadian rhythm regulating gene (CCA-1) in *Arabidopsis*. Wang et al is silent regarding any herbicide resistance gene, and does not report or suggest the use of a herbicide resistance gene in any the disclosed constructs. Further, the primary genetically engineered trait is a regulator of the circadian clock, was inserted for basic research on this clock, and with no perceived advantage to a crop.

Yet further, Wang et al is silent regarding any mitigating genetic trait detrimental to the uncultivated, interbreeding species, and not detrimental to a cultivated species of a cultivated crop is mentioned.

Yet further, Wang et al. report that the circadian clock rhythm protein CCA-1 is responsible for a wide variety of processes in plants:

> "There is a wide range of processes in plants that show a circadian rhythm. These include movement of organs such as leaves and petals, stomata opening, stem elongation, sensitivity to light of floral induction, metabolic processes such as respiration and photosynthesis, and expression of a large number of different genes (Bu, 1936; and reviewed by Piechulla, 1993; McClung and Kay, 1994; Anderson and Kay, 1996; Kreps and Kay, 1997). It is believed that the circadian rhythm of gene expression is part of the underlying mechanism for many, if not all, of the rhythms in metabolic and developmental processes."(Wang et al, page 1207, column 2)

Thus, in addition to the alterations of hypocotyl length and flower induction resulting from constitutive expression of the CCA-1 gene, as described in Wang et al., genetic modification of CCA-1 expression can be expected to disrupt numerous processes and functions in the plant grown as a crop. As such, the CCA-1 can hardly be characterized as a trait "...detrimental to an uncultivated, interbreeding species and not detrimental to a cultivated species of the crop...", as recited in amended claim 1. Thus, the CCA1 gene cannot be a mitigator gene, as it would have a deleterious effect on the crop.

Thus, Wang et al. fails to teach the essential features of a genetically engineered trait and a genetically linked, mitigating genetic trait, and transforming a population of plants of the cultivated crop to co-express the genetically engineered trait and the mitigating trait, and as such cannot and does not anticipate the invention as recited in amended claim 1, and claims dependent therefrom of the present invention.

The Examiner has further rejected claims 1-3 as being anticipated by Lee et al (US 5,948,956), asserting that Lee et al. teach methods for transforming cultivated turfgrass plants with a first gene encoding an herbicide resistance and a second gene encoding male sterility or dwarfism. Applicant disagrees.

Lee et al teaches a new method of transformation of grasses by biolistic transformation of node segments, and teaches the using of single genes, as genes of choice in such transformations. Such genes include genes for herbicide resistance, disease resistance, insect resistance, drought resistance, dwarfism, and the like. However, no combinations of desirable and mitigating traits are taught. Indeed, the Example disclosed details the success of the method in transforming turfgrass node segments with the CP4 or pat herbicide resistance genes, but no mention is made of the problem of unintentional transgene flow to uncultivated species, or methods for the mitigation of effects thereof. Indeed, it is the lack of the mitigating constructs described in this application in turfgrass that has caused widespread gene flow from experimental sites (see abstract by Reichman et al, attached), that has caused US APHIS to consider prohibiting the commercial release of material of the type described in Lee et al (see: http://www.aphis.usda.goc/biotechnology/brs_main.shtml).

Thus, Lee et al fails to teach the essential features of a genetically engineered trait and a genetically linked, mitigating genetic trait, and transforming a population of plants of the cultivated crop to co-express the genetically engineered trait and the mitigating trait, and as such cannot and does not anticipate the invention as recited in amended claim 1, and claims dependent therefrom of the present invention.

The abovementioned notwithstanding, to further distinguish the present invention from the cited references, and in order to expedite prosecution in this case, Applicant has chosen to amend claim 1 to include the limitations of:

(1) co-expression of the at least one advantageous genetically engineered trait, and the at least one mitigating genetic trait;

(2) tight genetically linkage of the advantageous and mitigating traits, so as to produce tandem introgression thereof; and

(3) introgression resulting in loss of fitness of the uncultivated species related to the genetically modified crop through expression of the mitigating genetic trait.

> "1.(Currently Amended) A method of obtaining a transformed, cultivated crop capable of mitigating the effects of introgression of at least one advantageous genetically engineered trait to an uncultivated interbreeding species related to the transformed cultivated crop, the method comprising transforming a population of plants of the cultivated crop to co-express the at least one advantageous

genetically engineered, trait, and at least one , mitigating genetic trait, wherein:

said advantageous genetic trait is selected beneficial to said crop;

said mitigating genetic trait is selected detrimental to the uncultivated interbreeding species and not detrimental to said crop;

whereas said advantageous genetically engineered trait and said mitigating genetic trait being tightly genetically linked so as to produce tandem introgression of said advantageous and said mitigating traits into said uncultivated interbreeding species; and

whereas introgression and expression of said mitigating genetic trait in said uncultivated interbreeding species related to the cultivated crop renders said uncultivated interbreeding species less fit compared to a similar uncultivated interbreeding species related to the cultivated crop and not expressing said mitigating genetic trait,

thereby obtaining a transformed cultivated crop capable of mitigating the effects of introgression of the at least one advantageous genetically engineered trait of said cultivated crop to the uncultivated interbreeding species related thereto.

Support for such an amendment can be found throughout the instant specification, for example, page 20, line 16 to page 23, line 5:

"One of the greatest advantages of herbicide-resistant crops is that they allow control of closely-related weeds that have the same herbicide selectivity spectrum as the crop and could not be previously controlled. Similarly, and advantage of disease and insect resistant crops is that they can be grown where there are secondary hosts, often close relatives, harboring the pests. Other resistant crops, e.g., cold resistance crops, are also of great advantage. Similarly, highly productive crops are advantageous, as are crops with modified product such as different types of starch and oils. Such and other genetic traits have been introduced into crops of various types by transgenics. These advantages of transgenics are fine, if there is no introgression into a relative weed or if the crop itself does not become a "volunteer" weed in subsequent crops. Because the advantages of transgenics are so great in the above cases, both industry and the farmers are clamoring for the transgenics."

Thus, it is applicant's opinion that such amendments are fully supported in the instant specification, and that no new material has been introduced.

Thus, it is Applicant's strong opinion that amended claim 1, and claims dependent therefrom, now more clearly define the essence of the method of the present invention, and as such overcome the Examiner's rejection thereof on the basis of the cited art references.

35 U.S.C. § 103(a) Rejections: MOGEN INTERNATIONAL (WO97/42326) in view of Christou et al (US. 6,114,603) and FORBIO RESEARCH (WO97/30162) in view of Boudet et al (US 5,451,514)

The Examiner has rejected claims 1-3, 7 and 8 under 35 U.S.C. § 103(a) as being unpatentable in view of MOGEN INTERNATIONAL (WO97/42326) in view of Christou et al (US. 6,114,603)(claims 1-3 and 7) and FORBIO RESEARCH (WO97/30162) in view of Boudet et al (US 5,451,514) (claims 1-3 and 8). Claims 1, 2 and 5-8 have been amended. The Examiner's rejections are respectfully traversed.

The Examiner has stated that MOGEN INTERNATIONAL teaches transformation of sugarbeet with an anti-bolting gene (TPP), and the use of herbicide resistance, and that Christou et al teach transformation of sugarbeets with bialaphos resistance, thus rendering obvious the method of the present invention for transformation of sugarbeets with a construct comprising an antibolting gene AND a bialaphos resistance gene. Applicant disagrees:

MOGEN INTERNATIONAL teaches the transformation of cells, incuding plant cells, with polynucleotides encoding trehalose-6-phosphate synthase (TPS) and trehalose-6-phosphate phosphatase (TPP), for affecting metabolic and other phenotypic changes in the host cells and organisms, such as altered leaf formation, enhanced photosynthesis, sterility, and the like. While reducing the invention to practice, plant species including tubers (potatoes), lettuce, beets, tomatoes, and the like were transformed with the TPS and TPP genes.

However, MOGEN INTERNATIONAL is silent regarding the subject of accidental, undesirable transgene flow from the transformed plants, and methods and/or constructs for the mitigation of the effects thereof. Further, the inclusion of a herbicide resistance gene is taught exclusively in the context of the method of transformation, as a marker gene, and the essential feature of tight genetic linkage between such an herbicide resistance gene and other sequences is specifically lacking:

> "To select or screen for transformed cells, it is preferred to include a marker gene linked to the plant expressible gene according to the invention to be transferred to a plant cell. The choice of a suitable marker gene in plant transformation is well within the scope of the average skilled worker; some examples of routinely used marker genes are the neomycin phosphotransferase genes conferring resistance to kanamycin (EP-B 131 623), the glutathion-S-transferase gene from rat liver conferring resistance to glutathione derived herbicides (EP-A 256 223), glutamine synthetase conferring upon overexpression resistance to glutamine synthetase inhibitors such as phosphinothricin (WO 87/05327), the acetyl transferase gene from Streptomyces viridochromogenes conferring resistance to the selective agent phosphinothricin (EP-A 275 957), the gene encoding a 5-enolshikimate-3-phosphate synthase (EPSPS) conferring tolerance to N-phosphonomethylglycine, the bar gene conferring resistance against Bialaphos (e.g. WO 91/02071) and the like. The actual choice of the marker is not crucial as long as it is functional (i.e. selective) in combination with the plant cells of choice.
> *The marker gene and the gene of interest do not have to be linked, since co-transformation of unlinked genes (U.S. Pat. No. 4,399,216) is also an efficient process in plant transformation.*"(MOGEN INTERNATIONAL, page 24, lines 3-23)

Thus, MOGEN INTERNATIONAL, alone or in combination with any other references, does not and cannot render the constructs and methods for their use of the claimed invention, lacking in novelty or obvious.

Similarly, Christou et al teaches methods for the biolistic transformation of sugarbeets:

> "In view of the foregoing, the present invention is directed to methods of making a genetically transformed sugarbeet plant comprising preparing a transgene; attaching the transgene to a substantially biologically inert carrier particle to form at least one coated particle; producing at least one cyclically regenerated sugarbeet shoot; and forcing the at least one coated particle into the at least one cyclically regenerated sugarbeet shoot."(Christou et al., Summary)

Christou et al further teaches that a herbicide resistance gene can be used along with the transformation of sequences of interest, as a selectable marker of

transformation (see Christou, Summary). However, as in MOGEN INTERNATIONAL, Christou et al is silent regarding the subject of accidental, undesirable transgene flow from the transformed plants, and methods and/or constructs for the mitigation of the effects thereof, and lacks any mention of the essential feature of tight genetic linkage between such an herbicide resistance gene and other sequences.

Thus, contrary to the Examiner's assertion, one of ordinary skill in the art would not be motivated to combine the methods for transformation with the TPS or TPP gene taught by MOGEN INTERNATIONAL with the methods of biolistic transformation of sugarbeets as disclosed by Christou et al, to produce the methods of obtaining a genetically modified, cultivated crop (of sugarbeets) capable of mitigating the effects of introgression of at least one advantageous genetically engineered trait to an uncultivated, interbreeding species related to the genetically modified crop, comprising the essential features of (1) co-expression of the at least one advantageous genetically engineered trait, and the at least one mitigating genetic trait; (2) tight genetically linkage of the advantageous and mitigating traits, so as to produce tandem introgression thereof; and (3) introgression resulting in loss of fitness of the uncultivated species related to the genetically modified crop through expression of the mitigating genetic trait.

The Examiner has further stated that claims 1-3 and 8 are rendered obvious by FORBIO RESEARCH in view of Boudet et al. Applicant disagrees.

FORBIO RESEARCH teaches the identification and cloning of reproductive-organ specific promoter elements from eucalypts, and their introduction into constructs for transformation of eukaryotic organisms, particularly plants and trees, with sequences of interest. One such construct disclosed includes the lethal barnase gene, under regulatory control of a MADS-box, tapetum-specific promoter. Prophetic experiments are discussed for the production of male-sterile transgenic eucalypt trees lacking all flowering and having enhanced harvestable timber content. No actual reduction to practice is disclosed.

Applicant wishes to point out that the production of such male-sterile plants fails to meet the criteria for preventing gene flow by mitigation in crops. Such male-sterile transgenic individual cannot pollinate relatives, however male sterility actually

promotes gene flow from the wild relatives, as the transgenic plants lack pollen for self-pollination, and thus more hybrids between transgenic and relatives will form in the male sterile plants than in the male sterile cultivars. Thus, the inhibition of flowering, and male sterility by expression of the cytotoxic barnase gene can be construed as neither an advantageous nor a benign mitigating trait in the transformed plants.

Further, FORBIO RESEARCH is silent regarding the subject of accidental, undesirable transgene flow from the transformed plants, and methods and/or constructs for the mitigation of the effects thereof, and the essential feature of tight genetic linkage between sequences for an advantageous and a mitigating trait is specifically lacking. Thus, FORBIO RESEARCH, alone or in combination with any other references, does not and cannot render the constructs and methods for their use of the claimed invention, lacking in novelty or obvious.

Boudet et al. teach the use of construct including a plant promoter and a sequence encoding a lignin precursor in an antisense orientation, for the suppression, in trees, of lignin biosynthesis, with the intent of producing timber with improved paper producing potential. Like FORBIO RESEARCH, Boudet et al is silent regarding the subject of accidental, undesirable transgene flow from the transformed plants, and methods and/or constructs for the mitigation of the effects thereof, and lacks any mention of the essential feature of tight genetic linkage between such a lignin-suppressor sequence and mitigating sequences.

Thus, contrary to the Examiner's assertion, one of ordinary skill in the art would not be motivated to combine the methods for transformation with the tapetum-promoter driven cytotoxic barnase gene taught by FORBIO RESEARCH with the lignin-supressor constructs as disclosed by Boudet et al, to produce the methods of obtaining a genetically modified, cultivated crop (of eucalypts) capable of mitigating the effects of introgression of at least one advantageous genetically engineered trait to an uncultivated, interbreeding species related to the genetically modified crop, comprising the essential features of (1) co-expression of the at least one advantageous genetically engineered trait, and the at least one mitigating genetic trait; (2) tight genetically linkage of the advantageous and mitigating traits, so as to produce tandem introgression thereof; and (3) introgression resulting in loss of

fitness of the uncultivated species related to the genetically modified crop through expression of the mitigating genetic trait.

In view of the above amendments and remarks it is respectfully submitted that claims 1, are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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Date: May 1, 2007

Encl.:
Petition for Extension of Time (3 Months)
Additional Claims Fee
Reichman et al, MOLECULAR ECOLOGY 15 (13): 4243-4255 NOV 2006; abstract